Remarks

Upon entry of the foregoing amendment, claims 1-11 are pending in the application, with claim 1 being the independent claims. Claims 1-4 are sought to be amended. Support for the amendment to claims 1-4 may be found, e.g., in Figure 1 and 2 of the specification, page 6, paragraph [0111], and throughout the published application. No new matter has been added by these amendments.

Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

Statement of Substance of Examiner Interview

On September 15, Applicants' representatives conducted a telephonic interview with Examiner Silverman. During the interview, the proper interpretation of claim 1 was discussed, and why the cited art did not anticipate or render obvious Applicants' claims. The Examiner's interview summary accurately reflects the substance of the interview. Applicants kindly thank Examiner Silverman for the courtesy extended during the interview, and for his very helpful comments and suggestions.

Obviousness-type Double Patenting Rejections

The Examiner rejected claims 1-11 for obviousness-type double patenting, over claims 16-30 of U.S. Patent No. 5,780,055 ("Habib"), in view of U.S. Patent No. 4,910,023 ("Botzolakis"). Applicants respectfully traverse this rejection.

Solely to advance prosecution, and not in acquiescence to the Examiner's rejection, Applicants have amended claim 1. The dosage form of claim 1 comprises an active cushioning component which is a bead, granule, particle or pellet comprising an active-loaded particle core surrounded by a porous cushioning layer. The active cushioning component is made by a process comprising admixing the core and cushioning materials followed by freeze-drying.

Claim 16 of the '055 patent recites a tablet comprising, *inter alia*, two separate beads, *viz.*, biologically active beads and cushioning beads, wherein the cushioning beads are prepared by extrusion-spheronization and freeze-drying.

Applicants respectfully submit, based on the reasons below under ***"Rejections under 35 U.S.C. § 103,"*** that claims 1-11 are nonobvious over the dosage form embodied in claims 16-30 of Habib in view of Botzolakis.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Rejections under 35 U.S.C. § 102

The Examiner rejected claims 1-11 under 35 U.S.C. 102(b) as allegedly anticipated by Mount *et al.* The Examiner further rejected claims 1-11 under 35 U.S.C. 102(a) as allegedly anticipated by Botzolakis. Applicants respectfully traverse these rejections.

Solely to advance prosecution, and not in acquiescence to the Examiner's rejection, Applicants have amended claim 1. Amended claim 1 recites a "porous" layer of placebo cushioning component that surrounds a core. Neither Mount *et al.*, nor Botzolakis disclose a compressible dosage form comprising an active cushioning

component having a porous cushioning layer surrounding a core. The porosity of the cushioning layer of Applicants' invention is created by the process of freeze-drying. See paragraph [0111] on page 6 of the published application. In freeze-drying, frozen liquid is removed from the particle by a sublimation process, i.e., a transition from a solid to a gaseous state, leaving behind a skeleton having pores formerly occupied by the frozen liquid, and relatively little, if any loss of volume to the particle. In contrast, oven-drying results in liquid evaporating from the particle, i.e., a transition from liquid to gas. The result is a more significant loss of volume, and consequently a much denser particle. Both Mount *et al.* and Botzolakis disclose particles that are oven-dried which does not produce a porous layer. Thus, the particles described by Mount *et al.* and Botzolakis are not "porous" as this term would be understood by a person having ordinary skill in the art, and the claims are clearly distinguished from the cited art. Thus, for at least these reasons, neither Mount *et al.*, nor Botzolakis anticipate the claimed invention.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejections

Rejections under 35 U.S.C. § 103

The Examiner rejected claims 1-11 under 35 U.S.C. § 103(a) as allegedly obvious over Botzolakis in view of Habib. Applicants respectfully traverse this rejection.

Based on the Supreme Court decision in *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007) ("*KSR*"), and current USPTO Examination Guidelines, the proper objective analysis for determining obviousness under 35 U.S.C. § 103 is as stated in *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966) ("*Graham*"). *See also*, Examination Guidelines for Determining Obviousness Under 35 U.S.C. § 103 in view of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.*, 72 Fed. Reg. 57526 (Oct. 10,

2007) ("*Examination Guidelines*"). Under this analysis, obviousness is a question of law based on underlying factual inquiries. The factual inquiries enunciated by the Court include: (1) determining the scope and content of the prior art; (2) ascertaining the differences between the claimed invention and the prior art; and (3) resolving the level of ordinary skill in the pertinent art. *KSR* did not remove the legally established requirement that each element of each claim must be taught in the documents cited by the Examiner. Additionally, the Court in *KSR* noted that the analysis supporting a rejection under 35 U.S.C. § 103(a) should be made explicit, and that it was "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the prior art elements" in the manner claimed. The Court specifically stated:

> [o]ften, it will be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. To facilitate review, this analysis should be made explicit.

KSR, at 1733 citing *In Re Kahn*, 441 F. 3d 977, 988 (Fed. Cir. 2006) ([Rejections on obviousness grounds cannot be sustained by mere conclusory statements, instead, there must be some articulated reasoning with some rational underpinning to support a legal conclusion of obviousness"). Additionally, in ascertaining the differences between the claimed invention and the prior art, it is well-established that a prior art reference must be considered in its entirety (i.e., as a whole), including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 220 USPQ 303 (Fed. Cir. 1983). *See also* MPEP § 2141.02(VI) and *Examination Guidelines* at 57528.

Considered as a whole, the art cited by the Examiner teach away from their combination. Botzolakis uses a water granulation method to load, *inter alia*, microcrystalline cellulose around a drug particle. Habib expressly notes that a water granulation method using microcrystalline cellulose produces weak compressible tablets and is therefore not acceptable. *See*, *e.g.*, col. 21, line 61 through col. 22, line 7; *See also*, col. 45, lines 17-22. Therefore, Habib disparages and discredits the method of making microcrystalline particles by water granulation, *i.e.*, the method of Botzolakis. Thus, one of ordinary skill would not combine the teachings of the cited art, and for at least this reason, the Examiner should withdraw the rejection.

Even if Habib were silent on the deficiencies of the method of Botzolakis, the combination would still not render the claimed invention obvious. Neither Habib, nor Botzolakis, either alone or in combination, teach freeze-drying the active-loaded particle core of the claims (either freeze-drying the active-loaded particle by itself, or in combination with a cushioning layer). While Habib makes a *general statement* that the means for making the biologically active loaded particle is not critical, and mentions various means for making particles, *Habib does not mention drying steps in the statement*:

> [t]he means for preparing the biologically active ingredient-loaded beads is not critical to the present invention. For example, the biologically active ingredient-loaded beads can be prepared by techniques well-known in the art such as, extrusion-spheronization, solution/suspension layering, powder layering, balling (a pelletization process in which finely divided particles are converted, upon the addition of appropriate quantities of liquid, to spherical particles by continuous rolling or tumbling action), or fluidized bed roto-granulation.

Col. 30, lines 39-48. This general statement in Habib, contrary to the Examiner's

assertions, is a far cry away from providing a reason to dry the drug particle by a freeze-drying method as required by the Applicants' claims. It is well known that compared with other, more conventional methods of drying, freeze-drying is very slow and uses complicated equipment, which is very expensive, especially compared with oven-drying. *See, e.g., Pharmaceutics: The Science of Dosage Form Design,* Edited by Michael E. Aulton, Churchill Livingstone, Edinburgh, London, Melbourne and New York, 1988, p 644.

Therefore, given Habib's general statement that the method for making the particle was not critical, the skilled artisan would have been motivated to use the easiest and most conventional means of drying the active-loaded drug particle. The skilled artisan would not have a reason to freeze-dry, for example, because it is much more cumbersome and more expensive than conventional methods.

Moreover, Applicants further contend that a person skilled in the art would have no reasonable expectation of success in arriving at a dosage form having the desired properties, even if there was a reason to freeze-dry the drug particle. Habib expressly points out that the method of drying affects the mechanical properties of spheres:

> [t]here is a remarkable difference in the physico-mechanical properties of pellets as a result of the drying technique. Kleinebudde (1994a), supra, compared freeze-drying, fluid-bed drying and oven drying. It was found that only a minor shrinking tendency can be seen during freeze-drying. Removing the water leaves a skeleton of solid materials with resultant freeze-dried pellets having similar size to the wet pellets, as well as high porosities. Evaporation of water in an oven or in a fluid bed is accompanied by a shrinking process. The resultant pellets are smaller than the wet ones, and are more dense.

Col 12, lines 47-57. Based on this disclosure, Applicants respectfully submit that the method of drying's effect on the mechanical properties of a drug particle would leave the

skilled artisan with no reasonable expectation that freeze-drying the drug-loaded particle, either by itself, or in concert with a layer of surrounding cushioning materials would produce a dosage form having the desired properties, especially in view of Habib's (or Botzolakis') lack of any disclosure of freeze-drying the active drug particles.

In view of the above, the properties of the dosage form of Applicants' invention could not have been predicted based on the teachings of the cited art. The dosage form of the invention comprises a non-segregatable, uniformly distributed active-loaded particle within a layer of cushioning material, which provides an unexpected cushioning characteristic such that coatings on active loaded particles can withstand a compression force during the tabletting process of as high as 1000 kg or more, for example.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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